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# PERSISTENT GASTROINTESTINAL SYMPTOMS AND CHRONIC FATIGUE AFTER SARS-COV-2 INFECTION.

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**Background/Aim:** Acute gastrointestinal infections are associated with an increased risk of developing functional gastrointestinal disorders and chronic fatigue syndrome. The digestive system is vulnerable to SARS-CoV-2 infection, but the point whether gastrointestinal symptoms and chronic fatigue persist after the infection has not been fully established. We have investigated the prevalence of gastrointestinal symptoms and chronic fatigue by means of a structured questionnaire after the resolution of SARS-CoV-2 infection. **Methods:** 378 subjects, age range 18-60 years, were studied. 177 patients had a molecular diagnosis of SARS-CoV-2 infection at our hospital in Feb-Apr 2020; 201 subjects, who had been tested because living in the same house as other infected people or working at the hospital, had a negative test in the same period (control group). 13 and 18 patients were respectively excluded because of a previous gastrointestinal disease, 9 and 16 of them with Irritable Bowel Syndrome (IBS). All the subjects filled in a web-based structured questionnaire about 5 months after infection. 164 patients (mean age 44 years, 40% female) and 183 control subjects (mean age 40 years, 61% female) completed the study. Their clinical data, acute SARS-CoV-2 related symptoms, the presence and severity of 22 gastrointestinal symptoms grouped in five symptom domains and the presence of six extra-intestinal symptoms including chronic fatigue were recorded according to the Structured Assessment of Gastrointestinal Symptoms (SAGIS) questionnaire. The Rome IV criteria for IBS, Bristol Stool scale, SCL 12 for somatoform disorders and HADS (Hospital Anxiety and Depression Scale) for anxiety and depression were also recorded. Association between exposure to SARS-CoV-2 infection and symptoms was evaluated by both univariate (chi-squared and Mann-Whitney tests) and multivariate analysis (linear and robust Poisson regression models). **Results:** Fever, shortness of breath, loss of smell and taste, fatigue, muscle pain, diarrhea, weight loss and antibiotic treatment were more frequent in patients during the infection (results not shown). After the infection resolving, the severity of abdominal pain/discomfort and diarrhea/incontinence symptoms was greater in patients than in controls (Table 1) as was the frequency of patients with chronic fatigue (31.7% vs. 13.7%;  $P < 0.001$ ). The frequency of IBS according to the Rome IV criteria, loose stools, SCL 12 for somatoform disorders and HADS -A and -D for anxiety and depression scores tended to be greater in patients than in controls (Table 2). **Conclusions:** The results of this controlled study show that abdominal pain/discomfort, diarrhea and chronic fatigue persist after SARS-CoV-2 infection in a significant proportion of patients. Our results suggest that SARS-CoV-2 may affect the brain-gut axis in the long term.

	Negative (n=183)	Positive (n=164)	p-value
SAGIS domain, (mean $\pm$ SD)			
- Abdominal pain/discomfort	0.33 $\pm$ 0.53	0.49 $\pm$ 0.60	0.0092
- Diarrhea/incontinence	0.28 $\pm$ 0.40	0.41 $\pm$ 0.55	0.0313
- Reflux disease/regurgitation	0.26 $\pm$ 0.44	0.39 $\pm$ 0.51	0.0617
- Nausea/vomiting	0.17 $\pm$ 0.35	0.2 $\pm$ 0.33	0.7616
- Constipation	0.35 $\pm$ 0.68	0.31 $\pm$ 0.62	0.8213

Table 1. Gastrointestinal symptoms in the five domains of the Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS) according to SARS-CoV-2 infection

	Negative (n=183)	Positive (n=164)	p-value
Irritable Bowel Syndrome (Rome IV), n (%)	46 (25.1%)	43 (26.2%)	0.81
Loose stool defined as Bristol $\geq 6$ , n (%)	17 (9.3%)	29 (17.8%)	0.02
SCL-12, (mean $\pm$ SD)	50.5 $\pm$ 10.8	54.6 $\pm$ 10.8	0.001
HADS-A, (mean $\pm$ SD)	4.47 $\pm$ 3.38	4.68 $\pm$ 3.97	0.87
HADS-D, (mean $\pm$ SD)	3.53 $\pm$ 3.34	3.81 $\pm$ 3.53	0.47

Table 2. Frequency of patients with IBS and loose stools and scores of Symptom Check List (SCL)-12 for somatization and of Hospital Anxiety and Depression Scale (HADS) according to previous SARS-CoV-2 infection.

# IMPACT OF COVID-19 RELATED DISRUPTIONS TO COLORECTAL CANCER SCREENING PROGRAMS IN THREE COUNTRIES: A COMPARATIVE MODELLING STUDY

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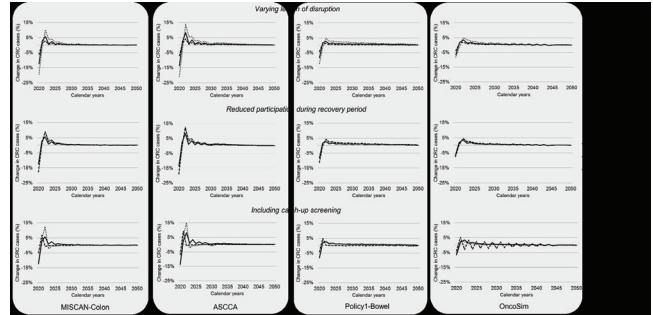
**Background** Colorectal cancer (CRC) screening programs worldwide have been disrupted during the COVID-19 pandemic. CRC screening has been well-established to reduce long-term CRC incidence and mortality. Any disruption to screening would reduce these health benefits. This study aimed to estimate the impact of hypothetical disruptions to organized CRC screening programs on short- and long-term CRC incidence and mortality in three countries using microsimulation modelling.

**Methods** Using well-calibrated and validated CRC microsimulation models for Australia (Policy1-Bowel), Canada (OncoSim) and the Netherlands (ASCCA and MISCAN-Colon) participating in the COVID-19 and Cancer Global Modelling Consortium (CCGMC), we simulated a range of hypothetical scenarios to assess the potential impact of disruptions to screening on CRC incidence and mortality. All models simulate the adenoma-carcinoma pathway, and ASCCA and Policy1-Bowel additionally simulate the serrated pathway. Modelled scenarios varied by disruption duration (3-, 6- and 12-months), post-disruption participation reduction (3-months -50% and 3-months -25%, and 6-months -50%), and catch-up screening strategies (no catch-up, immediate, and 6-months delayed catch-up).

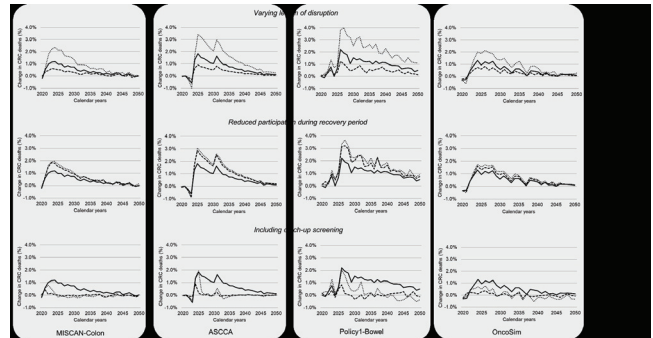
**Results** Without catch-up screening, CRC incidence would increase by 0.1-0.3%, 0.2-0.6%, and 0.4-1.2% over 2020-2050 among individuals aged 50 years and older in the three

modelled countries after 3-, 6-, and 12- month disruptions, respectively (Figure 1). CRC mortality would increase by 0.2-0.5%, 0.4-1.0%, and 0.8-2.0% over 2020-2050 among individuals aged 50 years and older in the three modelled countries after 3-, 6-, and 12-month disruptions, respectively, compared to undisrupted screening (Figure 2). A 6-month disruption without catch-up would result in an estimated 3,552, 2,844 and 803-1,803 additional CRC diagnoses and an estimated 1,964, 1,319, and 676-856 additional CRC-related deaths in Australia, Canada and the Netherlands, respectively, compared to undisrupted screening. A post-disruption reduction in participation could increase CRC diagnoses by 0.2-0.9% and CRC-related deaths by 0.5-1.6% compared to undisrupted screening depending on the size of the reduction in participation. Providing catch-up could minimize the impact of the disruption to an increase of 0.0-0.2% in CRC diagnoses and CRC-related deaths.

**Conclusion** Although the relative impact of the modelled CRC screening disruptions (when considered over the long-term, 30 years) due to the COVID-19 pandemic appears modest, given a high burden of CRC, there is a substantial impact on CRC diagnoses and deaths across all countries considered. It is crucial that, if disrupted, screening programs ensure participation rates return to previously observed rates and provide catch-up screening wherever possible, as the impact of any disruption could be considerably larger otherwise.



Change in CRC incidence relative to the comparator scenario (no disruption) by MISCAN-Colon, ASCCA, Policy1-Bowel and OncoSim Abbreviations: CRC, Colorectal Cancer. Note: the base case scenario is the scenario in which a 6-month disruption period from April to September 2020 was assumed, with no catch-up or changes to participation in the recovery period.



Change in CRC mortality relative to the comparator scenario by MISCAN-Colon, ASCCA, Policy1-Bowel and OncoSim Abbreviations: CRC, Colorectal Cancer. Note: the base case scenario is the scenario in which a 6-month disruption period from April to September 2020 was assumed, with no catch-up or changes to participation in the recovery period.

# CLINICAL COURSE OF PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS WITH POSITIVE COVID-19 ANTIBODY TESTING AT A SINGLE, TERTIARY CARE CENTER

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**Background:** The impact of SARS-CoV-2 infection on patients with IBD is still not fully understood. We aimed to evaluate the clinical course of pediatric IBD patients with positive COVID-19 antibody titers. **Methods:** This is a single-center, retrospective study of pediatric (<18y) IBD patients with positive COVID-19 Antibody Testing, using a serological enzyme-linked immunosorbent assay developed at Mount Sinai, Icahn School of Medicine. A COVID-19 Antibody Titer was sent routinely at time of biologic infusion or clinic visit between April and November 2020 to better understand IBD patients' seroconversion and long-term response to COVID-19. Data on demographics, disease behavior, location and activity (Harvey Bradshaw index or partial Mayo score) and treatment were gathered at time of antibody testing. Data were collected on antibody titer level (Amanat, F *et al. Nat Med* (2020) 26, 1033-1036) and, if available, on presence of symptomatic COVID-19 illness, worsening of IBD following SARS-CoV-2 infection, and changes to medications due to illness. Associations of COVID-19 symptom severity with biologic use and COVID-19 antibody titer were assessed with chi-square and Pearson product-moment correlation respectively. **Results:** Twenty-six children had a positive COVID-19 antibody test between May 6, 2020 and November 5, 2020; demographic, phenotype, and medication data are in Table 1. A majority (86%) of CD patients were in clinical remission, compared to only 1 (20%) UC patient. Median [IQR] antibody titer was 960 [320-1440]. Nineteen children (73%) had documentation regarding